The recommended dosage of efavirenz capsules is 600 mg orally, once daily, in combination with a protease inhibitor and/or nucleoside reverse transcriptase inhibitors (NRTIs). Precautions (5.7) should be sought immediately in patients developing severe rash associated with blistering, desquamation, or vesication. Efavirenz should be discontinued in patients developing severe rash and if symptoms persist after the dosage is reduced. Patients with rash should seek medical evaluation to assess the possibility that the symptoms may be related to the use of efavirenz. Administration of efavirenz can alter the concentrations of other drugs, and other drugs may alter the concentrations of efavirenz. The potential for drug-drug interactions must be considered before and during treatment.

As of July 2009, the Antiretroviral Pregnancy Registry has received prospective reports of 661 pregnancies exposed to efavirenz. Efavirenz is contraindicated in women who are or may become pregnant. Women of childbearing potential should use effective contraception for 1 month before treatment, throughout treatment, and for 1 month after treatment. Rash is the most common adverse effect, occurring in more than half of treated patients. The rash may be associated with gastrointestinal symptoms, headache, insomnia, tremors, anorexia, agitation, and other anxiety-related symptoms. Rash may be mild, moderate, or severe. Rash may be associated with hepatitis B or C coinfections, and patients with severe rash should discontinue therapy. One patient with rash and jaundice developed severe rash and required hospitalization.

Adverse Reactions (6.1) include rash, dizziness, nausea, headache, fatigue, insomnia, and vomiting. The most common adverse reactions (>5%, moderate-severe) are rash, dizziness, nausea, headache, fatigue, insomnia, and vomiting. (6) Includes erythema multiforme, rash, rash erythematous, rash follicular, rash maculopapular, rash petechial, rash pustular, and urticaria. Grade 3 rash Vesiculation, moist 0.8 1.8 0.3

Hepatic enzyme monitoring [see Precautions (5.7)] inclusion.

Calcium channel blocker No data are available on the potential interactions of efavirenz with other calcium channel blockers. Other compounds that are substrates of CYP3A may have decreased plasma concentrations after administration of efavirenz, but there is no evidence that efavirenz has a clinically significant effect on the pharmacokinetics of other CYP3A substrates.

Ethinyl estradiol/ Ethinyl estradiol/ethinyl estradiol [see Adverse Reactions (6.1, Table 4)]

There are insufficient data to make a dose recommendation for efavirenz.
of efavirenz is excreted unchanged in the urine, so the impact of renal impairment on efavirenz elimination should be minimal.

The pharmacokinetics of efavirenz in pediatric patients were similar to the adult population. The concentration of efavirenz in children was higher than in adults, but the overall exposure was similar. The pharmacokinetics of efavirenz were found to be consistent across different ethnic groups.

The metabolites are essentially inactive against HIV-1. The metabolism of efavirenz involves the cytochrome P450 system to hydroxylated metabolites with subsequent glucuronidation of these hydroxylated metabolites. These metabolites are not cytochrome P450 inducers, and therefore, efavirenz is not expected to cause hepatic enzyme induction, thus increasing the biotransformation of some drugs metabolized via the cytochrome P450 system.

Specific drug interaction studies have not been performed with efavirenz and NRTIs (e.g., lamivudine, zidovudine). Significant interactions would not be expected since the NRTIs are metabolized via a different route than efavirenz and would be unlikely to affect the clearance of efavirenz.

In vitro studies have shown that efavirenz is not a substrate or inhibitor of the CYP3A4 enzyme. However, in vivo studies have shown that efavirenz can inhibit the activity of CYP3A4 in some cases.

Efavirenz capsules contain the following inactive ingredients and dyes: silicon dioxide, sodium lauryl sulfate, gelatin, and yellow iron oxide. In addition, the capsules contain black edible ink filled with white to off-white colored powder.
Patient Information
Efavirenz Capsules
(efavirenz (eh-FAH-vih-rehnz))

ALERT: Find out about medicines that should NOT be taken with efavirenz capsules.

Read this information before you start taking efavirenz capsules. Read it again each time you refill your prescription, in case there is any new information. This leaflet provides a summary about efavirenz capsules and does not include everything there is to know about your medicine. This information is not meant to take the place of talking with your doctor.

What are efavirenz capsules?
Efavirenz capsules are a medicine used in combination with other medicines to help treat infection with Human Immunodeficiency Virus type 1 (HIV-1), the virus that causes AIDS (acquired immune deficiency syndrome). Efavirenz capsules are a type of anti-HIV drug called a "non-nucleoside reverse transcriptase inhibitor" (NNRTI). NNRTIs are not used in the treatment of Human Immunodeficiency Virus type 2 (HIV-2) infection.

Efavirenz capsules work by lowering the amount of HIV-1 in the blood (viral load). Efavirenz capsules must be taken with other anti-HIV medicines. When taken with other anti-HIV medicines, efavirenz capsules have been shown to reduce viral load and increase the number of CD4+ cells, a type of immune cell in blood. Efavirenz capsules may not have these effects in every patient.

Efavirenz capsules do not cure HIV or AIDS. People taking efavirenz capsules may still develop other infections and complications. Therefore, it is very important that you stay under the care of your doctor.

Efavirenz capsules have not been shown to reduce the risk of passing HIV to others. Therefore, continue to practice safe sex, and do not use or share dirty needles.

What are the possible side effects of efavirenz capsules?

Serious psychiatric problems. A small number of patients experience severe depression, strange thoughts, or angry behavior while taking efavirenz capsules. Some patients have thoughts of suicide and a few have actually committed suicide. These problems tend to occur more often in patients who have had mental illness. Contact your doctor right away if you think you are having these psychiatric symptoms, so your doctor can decide if you should continue to take efavirenz capsules.

Common side effects. Many patients have dizziness, trouble sleeping, drowsiness, trouble concentrating, and/or unusual dreams during treatment with efavirenz capsules. These side effects may be reduced if you take efavirenz capsules at bedtime on an empty stomach. They also tend to go away after you have taken the medicine for a few weeks. If you have these common side effects, such as dizziness, it does not mean that you will also have serious psychiatric problems, such as severe depression, strange thoughts, or angry behavior. Tell your doctor right away if any of these side effects continue or if they bother you. If it is possible that these symptoms may be more severe if efavirenz capsules are used with alcohol or mood altering (street) drugs.

If you are dizzy, have trouble concentrating, or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.

Rash is common. Rashes usually go away without any change in treatment. In a small number of patients, rash may become worse. If you develop a rash, call your doctor right away. Rash may be a serious problem in some children. Tell your child's doctor right away if you notice rash in some children.

Other common side effects include tiredness, upset stomach, vomiting, and diarrhea. Some patients taking efavirenz capsules have experienced increased levels of lipid (cholesterol and triglycerides) in the blood.

Changes in body fat. Changes in body fat develop in some patients taking anti-HIV medicine. These changes may include an increased amount of fat in the upper back and neck ("buffalo hump"), in the breasts, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these fat changes are not known.

Liver problems. Some patients taking efavirenz capsules have experienced serious liver problems including liver failure resulting in transplantation or death. Most of these serious side effects occurred in patients with a chronic liver disease such as hepatitis infection, but there have also been a few reports in patients without any existing liver disease.

Tell your doctor or healthcare provider if you notice any side effects while taking efavirenz capsules.

Contact your doctor before stopping efavirenz capsules because of side effects or for any other reason.

There is not a complete list of side effects possible with efavirenz capsules. Ask your doctor or pharmacist for a more complete list of side effects of efavirenz capsules and all the medicines you will take.

How should I take efavirenz capsules?
General Information

• You should take efavirenz capsules on an empty stomach, preferably at bedtime.
• Swallow efavirenz capsules with water.
• Taking efavirenz capsules with food increases the amount of medicine in your body, which may increase the frequency of side effects.
• Taking efavirenz capsules at bedtime may make some side effects less bothersome.
• Efavirenz capsules must be taken in combination with other anti-HIV medicines. If you take only efavirenz capsules, the medicine may stop working.
• Do not miss a dose of efavirenz capsules. If you forget to take efavirenz capsules, take the missed dose right away, unless it is almost time for your next dose. Do not double the next dose. Carry on with your regular dosing schedule. If you need help in planning the best times to take your medicine, ask your doctor or pharmacist.
• Take the exact amount of efavirenz capsules your doctor prescribes. Never change the dose on your own. Do not stop this medicine unless your doctor tells you to stop.
• If you believe you took more than the prescribed amount of efavirenz capsules, contact your local Poison Control Center or emergency room right away.
• Talk to your doctor if you start any new medicine or change how you take old ones. Your doses may need adjustment.
• When your efavirenz capsules supply starts to run low, get more from your doctor or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to efavirenz and become harder to treat.
• Your doctor may want to do blood tests to check for certain side effects while you take efavirenz capsules.
• The dose of efavirenz capsules for adults is 600 mg (three 200 mg capsules, taken together) once a day by mouth. The dose of efavirenz capsules for children may be lower (see Can children take efavirenz capsules?).

Can children take efavirenz capsules?
Yes, children who are able to swallow capsules can take efavirenz capsules. Rash may be a serious problem in some children. Tell your child's doctor right away if you notice rash or any other side effects while your child is taking efavirenz capsules. The dose of efavirenz capsules for children may be lower than the dose for adults. Capsules containing lower doses of efavirenz are available. Your child's doctor will determine the right dose based on your child's weight.

Who should not take efavirenz capsules?

Do not take efavirenz capsules if you are allergic to the active ingredient, efavirenz, or to any of the inactive ingredients. Your doctor and pharmacist have a list of the inactive ingredients.

What should I avoid while taking efavirenz capsules?

• Women should not become pregnant while taking efavirenz capsules and for 12 weeks after stopping them. Serious birth defects have been seen in the offspring of women treated with efavirenz capsules during pregnancy. It is not known whether efavirenz capsules cause these defects. Tell your doctor right away if you are pregnant. Also talk with your doctor if you want to become pregnant.
• Women should not rely only on hormone-based birth control, such as pills, injections, or implants, because efavirenz capsules may make these contraceptives ineffective. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control. Efavirenz may remain in your blood for a time after therapy is stopped. Therefore, you should continue to use contraceptive measures for 12 weeks after you stop taking efavirenz capsules.

• Do not breast-feed if you are taking efavirenz capsules. The Centers for Disease Control and Prevention recommend that mothers with HIV not breast-feed because they can pass the HIV through their milk to the baby. Also, efavirenz may pass through breast milk and cause serious harm to the baby. Talk with your doctor if you are breast-feeding. You may need to stop breast-feeding or use a different medicine.

• Efavirenz capsules with alcohol or other medicines causing similar side effects as efavirenz capsules, such as drowsiness, may increase those side effects.

• Do not use other medicines without checking with your doctor. These medicines include prescription and nonprescription medicines and herbal products, especially St. John’s wort (Hypericum perforatum).

Before using efavirenz capsules, tell your doctor if you
• have problems with your liver or have hepatitis. Your doctor may want to do tests to check your liver while you take efavirenz capsules or may switch you to another medicine.

• have ever had mental illness or are using drugs or alcohol.

• have ever had seizures or are taking medicine for seizures (for example, Dilantin (phenytoin), Teregrel (carbamazepine), or phenobarbital). Your doctor may want to switch you to another medicine or check drug levels in your blood from time to time.

What important information should I know about taking other medicines with efavirenz capsules?

Efavirenz capsules may change the effect of other medicines, including ones for HIV, and cause serious side effects. Your doctor may change your other medicines or change their doses. Other medicines, including herbal products, may affect efavirenz capsules. For this reason, it is very important to:

• let all your doctors and pharmacists know that you take efavirenz capsules.

• tell your doctors and pharmacists about all medicines you take. This includes those you buy over-the-counter and herbal or natural remedies. Bring all your prescription and nonprescription medicines as well as any herbal remedies that you are taking when you see a doctor, or make a list of their names, how much you take, and how often you take them. This will give your doctor a complete picture of the medicines you use. Then he or she can decide the best approach for your situation.

Taking efavirenz capsules with St. John’s wort (Hypericum perforatum), an herbal product sold as a dietary supplement, or products containing St. John’s wort is not recommended. Talk with your doctor if you are taking or are planning to take St. John’s wort. Taking St. John’s wort may decrease efavirenz levels and lead to increased viral load and possible resistance to efavirenz or cross-resistance to other anti-HIV drugs.

MEDITCES YOU SHOULD NOT TAKE WITH EFAVIRENz CAPSULES

The following medicines may cause serious and life-threatening side effects when taken with efavirenz capsules. You should not take any of these medicines while taking efavirenz capsules:

• Vascor (bepridil)

• Propulsid (cisapride)

• Versed (midazolam)

• Orap (pimozide)

• Halcion (triazolam)

• Ergot medications (for example, Wigraine and Catergot)

The following medicine should not be taken with efavirenz capsules since they contain efavirenz, the active ingredient in efavirenz capsules:

• ATRIPRA (efavirenz, emtricitabine, tenofovir disoproxil fumarate)

The following medicines may need to be replaced with another medicine when taken with efavirenz capsules:

• Fortovase, Invirase (saquinavir)

• Biaxin (clarithromycin)

• Carbamol, Teregrel (carbamazepine)

• Naxaflo (posaconazole)

• Mycobutin (rifabutin)

• REYATAZ (atazanavir sulfate), if this is not the first time you are receiving treatment for your HIV infection.

The following medicines may require a change in the dose of either efavirenz capsules or the other medicine:

• Calcium channel blockers such as Cardizem or Ticaz (diltiazem), Covera HS or Isoptin SR (verapamil), and others.

• The cholesterol-lowering medicines Lipitor (atorvastatin), PRAVACHOL (pravastatin sodium), and Zocor (simvastatin).

• Crixivan (indinavir)

• Kaetra (lopinavir/ritonavir)

• Methadone

• St. John’s wort

• The immunosuppressant medicines cyclosporine (Gengraf, Nocoral, Sandimmune, and others), Prograf (tacrolimus), or Rapamune (sirolimus).

These are not all the medicines that may cause problems if you take efavirenz capsules. Be sure to tell your doctor about all medicines that you take.

General advice about efavirenz capsules:

- Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use efavirenz capsules for a condition for which it was not prescribed. Do not give efavirenz capsules to other people, even if they have the same symptoms you have. They may harm them.

- Keep efavirenz capsules at room temperature 20° to 25°C (68° to 77°F) in the bottle given to you by your pharmacist. The temperature can range from 15° to 30°C (59° to 86°F).

- Keep efavirenz capsules out of the reach of children.

This leaflet summarizes the most important information about efavirenz capsules. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for the full prescribing information about efavirenz capsules or you can call 1-866-850-2876.

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